REMARKS

Upon entry of the present amendment, claims 1-14, 16, 20, 25-33, and 53-55 will be pending in the present application. Applicants have cancelled claims 34-52, 56, and 57 without prejudice or disclaimer; pending claims 10, 14, 26-33, and 53-55 have been withdrawn from consideration, leaving claims 1-9, 11 -13, 16, 20, and 25 currently under consideration.

Applicants' Summary of Telephone Interview

As an initial matter, Applicants wish to thank Examiner Jung for the courtesy of the telephone conference on September 1, 2009, with the undersigned and inventor Larry Stern. The pending rejections under 35 U.S.C. 103 were discussed.

Prematurity of Finality of Office Action

Applicants note that, per MPEP 706.07(a),

> ... second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims, nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p).

As the Examiner withdrew all of the previously pending rejections (see pages 2-3 of the Office Action mailed May 12, 2009 (the "Office Action")), and issued an entirely new set of rejections that was neither based on the Applicants' amendments nor based on information submitted in an IDS, Applicants submit that the finality of the present action was premature. Applicants therefore request that the finality of this action be withdrawn, and further request a refund of the fees for the Request for Continued Examination submitted herewith.

Withdrawn Objections

Applicants note with appreciation that the Examiner has withdrawn the previously pending rejections under 35 U.S.C. 103.

Rejections under 35 U.S.C. 103

Claims 1-7, 11, 12, 16, 20, and 25 were rejected as allegedly obvious over Webb et al. (WO 97146256, Dec. 11, 1997, "Webb") in view of Rhode et al. (U.S. Patent No. 6,232,445, May 15, 2001, "Rhode"), Lehmann et al. (U.S. Patent No. 5,939,281, Aug. 17, 1999, "Lehmann"), Yurino et al. (U.S. Patent No. 6,127,125, Oct. 3, 2000, "Yurnino"), and Alfenito (U.S. Patent No. 6,355,419 B1, Mar. 12, 2002, "Alfenito"). Applicants respectfully traverse.

The Examiner relies on Webb as a primary reference for teaching arrays of MHC-peptide complexes. As the Examiner conceded,

> Webb et al. is silent on disclosing that the each group of spatially distinct areas comprises a plurality of different MHC-peptide complexes and that the array, further comprises anti-factor antibodies specific for secreted factors, immobilized spatially-distinct areas on the substrate. Webb et al. further fails to teach that the substrate is flat. Finally, Webb et al. fails to teach that at least one hydrophobic barrier surrounds a plurality of the spatially-distinct areas and each of the spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier, such that when a single volume of sample is applied inside of the at least one hydrophobic barrier, all areas in the plurality of said spatially-distinct areas are in contact with the single volume of sample.

See page 6 of the Office Action. The Examiner further cites Rhode for the use of arrays of MHC complexes to screen immune cells. The "arrays" disclosed in Rhode are 96-well plates; as one of skill in the art would appreciate, such plates do not meet the limitations of claim 1 as each spatially-distinct area in a 96-well plate is surrounded by a barrier. Furthermore, in the arrays described in Rhode et al., there are no immobilized anti-factor antibodies as recited in part (ii) of claim 1, and cytokine release is detected in supernatants removed from the plates after stimulation. Thus the method of Rhode relies on diffusion of cytokines released from the cells into the general solution.

Lehmann is also cited by the Examiner; Lehmann teaches cytokine capture assays performed in microwell plates. Again, as one of skill in the art would appreciate, such plates do not meet the limitations of claim 1 as each spatially-distinct area in a microwell plate is surrounded by a barrier. In the assay methods described in Lehmann et al., the cells are removed from the plate after stimulation, and the assay performed on the plate; each microwell represents a single reaction.

The Examiner cites Yurino as allegedly teaching a biochip "comprising a plurality of regions bound with various probes" in which a sample can be applied to "the entire features of the biochip." Applicants note that Yurino relates to methods for using centrifugal force for applying a sample of nucleic acid to a biochip comprising nucleic acid probes, and makes no mention of use with living cells or proteins.

Further, Alfenito is cited as teaching a nylon membrane with

> ... a plurality of subarrays of probes on the nylon membrane, the subarrays comprising a plurality of individual spots wherein each spot is comprised of a plurality of probes of the same sequence; and a plurality of hydrophobic barriers located between the subarrays on the nylon membrane, whereby the plurality of hydrophobic barriers prevents cross contamination between adjacent subarrays (see entire document, particularly column 3, lines 5-14). Many samples may be interrogated as pools at the same subarrays or independently with different subarrays within one support (column 35, lines 55-63).

See page 7 of the Office Action. The Examiner concluded at page 9 of the Office Action that

> ...it would have been obvious to one of ordinary skill in the art at the time of the invention to provide at least one hydrophobic barrier surrounding a plurality of the spatially-distinct areas (each of the spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier) such that when a single volume of sample is applied inside of the at least one hydrophobic barrier, all areas in the plurality of said spatially distinct areas are in contact with the single volume of sample as taught by Alfenito in the array of Webb et al. in view of Rhode et al., Lehmann et al., and Yurino et al. in order to prevent cross contamination between adjacent subarrays for simultaneous analysis of multiple samples. The advantage of analyzing multiple samples simultaneously with cross contamination provides the motivation to combine teachings of Webb et al. in view of Rhode et al., Lehmann et al., and Yurino et al. and Alfenito with a reasonable expectation of success."

As a first matter, Applicants note that both Yurino and Alfenito relate to arrays of nucleic acids, while Webb et al., Lehmann et al., and Rhode (and the present arrays) relate to assays in which live cells are used. As one of skill in the art will appreciate, assay conditions that are acceptable or desirable for isolated nucleic acids are not necessarily directly or readily transferable to assays in which live cells are used. Although all of the cited art might generally fall under the category of "biological assays," Alfenito and Yurino are non-analogous art; thus, one of skill in the art would not have been motivated to take the teachings of Webb, Lehmann, and/or Rhode in

combination with either or both of Yurino or Alfenito. Thus, there would be no motivation to combine the two.

In addition, and more importantly, there would have been no reasonable expectation of success in making such a combination. See the DECLARATION OF LAWRENCE J. STERN, PH.D., which notes that given the time course of the experiments, the size of the molecules, one of skill in the art would not have had a reasonable expectation of success in using the arrays as recited in the pending claims. The nucleic acid binding methods described in Yurino or Alfenito rely on molecular binding interactions that are quite stable over the time frame of the assay (generally on the order of minutes); the nucleic acid binds specifically to a probe, and essentially remains bound to the probe for the duration of the assay (or, if unbinding occurs, re-binding rapidly occurs). This tight binding allows for the washing away of unbound reactants, etc., and reduces the possibility of non-specific binding of reactants. In contrast, in the case of the methods for which the presently claimed arrays are configured, the assay takes place over a period of many hours to days; the living cells in the assay would be expected to diffuse through the media and, once activated, secrete the cytokines into the general solution. Given the long time frame of the assay, one of skill in the art would expect that the diffusion of the T cells and secreted cytokines into the solution would result in such an immense amount of background staining that the individual areas would be indistinguishable, and that the arrays would be useless for identifying from which cell the cytokines are secreted. As demonstrated in the present application, this surprisingly is not the case; see the Examples and Figures.

Thus, for at least the reasons set forth above, the cited art fails to teach or suggest the recited arrays at least in failing to disclose an array that, as recited in claim 1, has

> ... at least one hydrophobic barrier that surrounds a plurality of said spatially-distinct areas; and each of said spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier, such that when a single volume of sample is applied inside of the at least one hydrophobic barrier, all areas in the plurality of said spatially-distinct areas are in contact with the single volume of sample, and wherein at least one of the spatially-distinct areas comprises a plurality of MHC-peptide complexes that are different from the MHC-peptide complexes of at least one other spatially-distinct area.

For further explication of these arguments, Applicants direct the Examiner's attention to Applicants' AMENDMENT IN REPLY TO ACTION OF APRIL 9, 2007 (see, e.g., pages 15-

16), AMENDMENT IN REPLY TO ACTION OF DECEMBER 27, 2007 (see, e.g., pages 15-16), and AMENDMENT IN REPLY TO ACTION OF JULY 22, 2008 (see, e.g., pages 12-13).

Claims 8 and 9 were rejected as allegedly obvious over Webb (WO 97146256, Dec. 11, 1997, "Webb") in view of Rhode (U.S. Patent No. 6,232,445, May 15, 2001, "Rhode"), Lehmann (U.S. Patent No. 5,939,281, Aug. 17, 1999, "Lehmann"), Yurino (U.S. Patent No. 6,127,125, Oct. 3, 2000), and Alfenito (U.S. Patent No. 6,355,419 B1, Mar. 12, 2002) as applied to claim 1 above, and further in view of Tom-Moy et al. (U.S. Patent No. 6,235,488, May 22, 2001 ("Tom-Moy")). Applicants respectfully traverse; for at least the reasons set forth above; Tom-Moy (which the Examiner cites for the use of streptavidin) does not supply the motivation to combine or the reasonable expectation of success missing from the other references as described above.

Claim 13 was rejected as allegedly obvious over Webb (WO 97146256, Dec. 11, 1997, "Webb") in view of Rhode (U.S. Patent No. 6,232,445, May 15, 2001, "Rhode"), Lehmann (U.S. Patent No. 5,939,281, Aug. 17, 1999, "Lehmann"), Yurino (U.S. Patent No. 6,127,125, Oct. 3, 2000, "Yuri), and Alfrenito (U.S. Patent No. 6,355,419 B1, Mar. 12, 2002) as applied to claims I, 1 I, and 12 above, and further in view of Abraham et al. (J. Immunol., 2001 4, Vol. 167, pp5193-5201) and Mikesell et al. (U.S. PG Pub. No. US 200210095024, Filed on June 6, 2001). Applicants respectfully traverse.

Applicants respectfully traverse; for at least the reasons set forth above; Abraham and Mikesell simply do not supply the motivation to combine or the reasonable expectation of success missing from the other references as described above.

For at least the reasons set forth above, Applicants submit that the pending claims are not obvious over the cited art, and request withdrawal of the rejections under 35 U.S.C. § 103. All of the dependent claims are patentable for at least similar reasons as those for the claims on which they depend are patentable. Applicants respectfully note that, according to MPEP § 2145, "[evidence] pertaining to secondary considerations must be taken into account whenever present ... If the evidence is deemed insufficient to rebut the prima facie case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify this conclusion."

The Examiner is invited to telephone the undersigned should it be deemed likely to expedite allowance of the present case.

The Petition for Extension of Time fee is being paid on the electronic filing system by way of deposit account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing attorney docket 07917-0212001.

Respectfully submitted,

Date: Nov 12, 2009

Janice Kugler DeYoung
Reg. No. 50,429

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (877) 769-7945